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毛梗希莶的化学成分*

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摘要 从毛梗希莶(*Siebesbeckia glabrescens*)的乙醇提取物中分到胡萝卜甙和3个二萜类成分, 根据光谱和化学证据, 3个二萜的化学结构被分别确定为: 对映－16β,17—二羟基贝壳杉烷—19—酸(1), 腺梗希莶甙(2)和希莶甙(3)。对映二羟基—16β,17—贝壳杉烷—酸和腺梗希莶甙系首次从毛梗希莶中到。

关键词 菊科, 毛梗希莶, 对映—16β,17—二羟基贝壳杉烷—19—酸(1), 腺梗希莶甙(2), 希莶甙(3)
分类号 Q946

The Constituents of Siegesbeckia glabrescens

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Abstract Three diterpenoids, compound A (1), B (2) and C (3), have been isolated together with daucosterol (4) from the ethanol extract of *Siegesbeckia glabrescens*. Their chemical structures have been elucidated as ent—16β,17—dihydroxykauran—19—oic acid (1), siegesbeckioside (2), darutoside (3),on the basis of chemical and spectral evidences. Compounds 1 and 2 are isolated for the first time from *Siegesbeckia glabrescens*.

Key words Compositae, *Siegesbeckia glabrescens*, ent—16β,17—dihydroxykauran—19—oic acid (1), Siegesbeckioside(2), Darutoside (3)

Plants of the genus *Siegesbeckia* are annual herbs widely distributed in tropical and temperate zones, and they have been used as a traditional medicine to treat rheumatic arthritis, hypertension, malaria, neurasthenia and snake—bite in China. Modern pharmacological experiments show that the extracts and constituents of *Siegesbeckia* exhibit analgesic, antiinflammatory(Yamatomo *et al*, 1987), antihypertensive(Kim *et al*, 1980), antioxidative(Su *et al*, 1986), immuno—inhibitory, and infertile activities(Dong *et al*, 1989; Ynag *et al*, 1976). A series of ent—kaurane and ent—pimarane diterpenoids(Xiong *et al*, 1992, 1997; Liu *et al*, 1991; Kim *et al*, 1979), sesquiterpene lactones, and flavonoids from *Siegesbeckia* have been reported(Zdero *et al*, 1991). In our continuing search for biologically active constituents from *Siegesbeckia* plants, five new diterpenoids have been reported previously(Xiong *et al*, 1992, 1997). The present paper describes the isolation, structural elucidation and identification of the other three diterpenoids from *Siegesbeckia glabrescens*.

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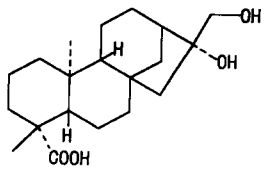
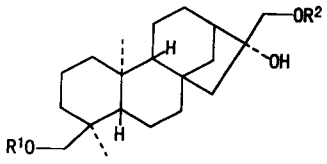
RESULTS AND DISCUSSION

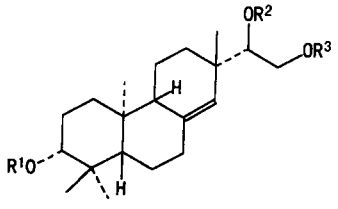
Compound A (1) $C_{20}H_{32}O_4$, *M* 336, was obtained as colourless plates. Its IR spectrum revealed that hydroxyl (3420, 3250, 1027 cm^{-1}) and carboxyl (1690 cm^{-1}) were present as functional groups. 1 showed the presence of two methyl groups, ten methyene groups, three methine groups, four quaternary carbons, and one carboxyl group in the ^{13}C NMR spectrum (Table 1). The above data and two tertiary methyl signals at δ1.19, 1.35 ppm and 5 unsaturation degrees suggested that 1 has a typical ent-kaurane nucleus as basic skeleton (Xiong *et al*, 1992). In the ^{13}C NMR spectrum of 1, two singlets (δ44.03, 180.19 ppm) and one quartet (δ29.43 ppm) are reasonably assigned to C-4, C-19 and C-18. The signals at (4.13 and 4.04 (each 1H, d, 10.8Hz) and at δ46.02 (d), 54.01 (t), 81.73 (s) and 66.53 (t), assigning to C-13, C-15, C-16 and C-17, indicated the presence of two-substituted 16α,17-glycol system. Therefore, the chemical structure of 1 can be represented as ent-16β,17-dihydroxy-kauran-19-oic acid (1).



1



	R1	R2
2	Glc	H
2a	Glc(Ac)$_4$	Ac



	R1	R2	R3
3	Glc	H	H
3a	Glc(Ac)$_4$	Ac	Ac

Compound B (2) $C_{26}H_{44}O_8$, M 484, was obtained as colourless needles. Its IR spectrum (3575, 3510, 3380, 1080, 1049, 1020 cm^{-1}) revealed the presence of hydroxyl groups. 2 showed the presence of two methyl groups, eleven methyene groups, three methine groups, four quaternary carbons, and one glucose moiety in the ^{13}C NMR spectrum (Table 1). The above data and two tertiary methyl signals at (1.00, 0.79 ppm and 5 unsaturation degrees suggested that 2 has a typical ent-kaurane nucleus as basic skeleton (Xiong *et al*, 1992). In the ^{13}C NMR spectrum of 2, one singlet (δ37.65 ppm), one quartet (δ17.97 ppm) and one extreme downfield triplet (δ79.47 ppm) are reasonably assigned to C-4, C-19 and C-18. This suggestion is supported by the signals at 3.75, 3.42 (each 1H, d, 9.52 Hz). The signals at δ4.13, 4.04 (each 1H, d, 10.8 Hz) and at δ46.13 (d), 54.15 (t), 81.64 (s) and 66.52 (t), assigning to C-13, C-15, C-16 and C-17, indicated the presence of two-substituted 16α,17-glycol system. The signals at δ4.80 (1H, d, 7.76 Hz) and δ105.58 (d) were assignable to C-1 position of glucose, thus suggesting the β-configuration at the anomeric carbon of the glucoside. Other signals of 2 at δ4.61 (1H, dd, 11.64, 1.88 Hz), 4.46 (1H, dd, 11.64, 5.20 Hz), 4.30～4.23 (2H, m), 4.09～4.00 (2H, m) and at (75.26 (d), 78.53 (d), 71.86 (d), 78.67 (d), 62.96 (t) were in agreement with those of the β-D-glucoside. Furthermore, the signal assignable to C-18 (δ79.47 t) of **2** was unchanged in comparison

with that of the pentaacetate **2a**. Accordingly, the chemical structure of 2 can be determined as ent—16β,17,18—trihydroxykauran—18—O—β—D—glucopyranoside, namely siegesbeckioside (2).

Table 1　^{13}C NMR chemical shifts of 1, 2, 2a, 3 and 3a in C_5D_5N

Carbon	1	2	2a	3	3a
1	41.18 t	40.00 t	40.00 t	37.14 t	36.75 t
2	19.92 t	18.36 t	18.18 t	24.17 t	23.87 t
3	38.86 t	36.42 t	36.01 t	85.32 d	86.17 d
4	44.03 s	37.65 s	37.36 s	38.77 s	38.73 s
5	57.18 d	49.28 d	49.66 d	55.08 d	54.99 d
6	23.03 t	20.74 t	20.87 t	22.73 t	22.67 t
7	42.88 t	42.02 t	42.11 t	36.46 t	36.27 t
8	45.06 s	44.88 s	44.95 s	138.39 s	140.76 s
9	56.46 d	56.92 d	57.20 d	50.90 d	50.71 d
10	41.15 s	39.45 s	39.41 s	38.21 s	38.36 s
11	19.07 t	18.73 t	18.30 t	18.87 t	18.86 t
12	26.84 t	26.89 t	26.76 t	32.93 t	32.74 t
13	46.02 d	46.13 d	46.57 d	38.10 s	37.43 s
14	37.87 t	37.90 t	37.70 t	129.53 d	126.93 d
15	54.01 t	54.15 t	54.07 t	76.82 d	74.97 d
16	81.73 s	81.64 s	78.99 s	64.04 t	64.11 t
17	66.53 t	66.52 t	69.32 t	23.40 q	23.50 q
18	29.43 q	79.47 t	79.26 t	29.02 q	28.82 q
19	180.19 s	17.97 q	17.73 q	14.97 q	14.84 q
20	16.12 q	18.51 q	18.30 q	17.29 q	16.85 q
Glc—1′		105.58 d	101.38 d	102.45 d	99.20 d
—2′		75.26 d	72.30 d	75.22 d	72.35 d
—3′		78.53 d	73.60 d	78.20 d	73.69 d
—4′		71.86 d	69.40 d	72.18 d	69.82 d
—5′		78.67 d	72.22 d	78.64 d	72.35 d
—6′		62.96 t	62.54 t	63.34 t	62.79 t
OAc			171.17 s		170.79 s
			170.48 s		170.71 s
			170.29 s		170.58 s
			169.81 s		170.48 s
			169.42 s		169.98 s
			20.87 q		169.59 s
			20.66 q		20.98 q
			20.58 q		20.76 q
			20.45 q		20.76 q
			20.45 q		20.76 q
					20.62 q
					20.62 q

Compound C (3)　$C_{26}H_{44}O_8$, M 484; white amorphous powder. Its IR spectrum revealed that hydroxyl (3400～3360, 1072, 1025, 1010 cm^{-1}) and double bond (1630 cm^{-1}) were present as functional groups. 3 showed the presence of four methyl groups, seven methyene groups, four methine groups, three quaternary carbons, two olefinic carbons and one glucose moiety in the ^{13}C NMR spectrum (Table 1). The above data and four tertiary methyl signals at δ1. 19, 1.14, 0.88, 0.67 ppm and 5 unsaturation degrees suggested that 3 has a typical *ent—pimarane* nucleus as basic skeleton (Dong *et al*, 1989). In the ^{13}C NMR spectrum of 3, one singlet (δ38.77 ppm), one Extreme downfield doublet (δ85.32 ppm), and two quartets (δ29.02, 14.97 ppm) are reasonably assigned to C—4, C—3, C—18 and C—19. The glucose is linked to 3α position based on the

above data and the signal at 3.52 (dd, 11.58, 3.50 Hz). The signals at δ38.10 (s), 76.82 (d), 64.04 (t) and 23.40 (q) assigning to C—13, C—15, C—16 and C—17, indicated the presence of one—substituted 15,16—glycol system. The signals at δ4.84 (1H, d, 7.68 Hz) and δ102.45 (d) were assignable to C—1 position of glucose, thus suggesting the β—configuration at the anomeric carbon of the glucoside. Other signals of 3 at δ4.51 (1H, dd, 9.84, 1.88 Hz), 4.51～4.33 (2H,m), 4.33 (1H, dd, 11.32, 5.24 Hz), 4.21～3.91 (2H, m) at δ75.22 (d), 78.20 (d), 72.18 (d), 78.64 (d), 63.34 (t) were in agreement with those of the β—D—glucoside. Furthermore. the signal assignable to C—3 (δ85.32, d) of 3 was unchanged in comparison with that of the hexaacetate **3a**. Accordingly, the chemical structure of 3 can be determined as *ent*—3β,15,16—trihydroxypimaran—3—O—β—D—glucopyranoside, namely, darutoside (3).

EXPERIMENT

General Kofler melting points were uncorrected; Optical rotations were taken on a Jasco—20C digital polarimeter. IR were recorded on KBr discs with a Perkin—Elmer 577 spectrometer. UV were obtained in EtOH on a UV—210A spectrometer. EIMS (positive) were measured on a VG Auto Spec—3000 spectrometer with direct inlet 70 or 20 eV. NMR were run on a Brucker AM—400 specrtometer using TMS as internal. standard; chemical shift values are reported in ((ppm) units (pyridine—d5). Coupling constants (J) were expressed in Hz.

Plant Material *Siegesbeckia glabrescens* was collected in Fumin County, Yunnan, China in Sept,1992 and identified by Prof. Yanhui Li. A voucher specimen was deposited in the Herbarium of Kunming Institute of Botany, Academia Sinica.

Extraction and isolation Dried and powdered herbs (7.76 kg) were repeatedly soaked with warm EtOH for 2 days × 4 and then concd. to crude residue. The residue was suspended in H_2O and shaken, in order, in EtOAc (×3), and n—BuOH (×4) saturated with H_2O. The EtOAc soln was evapd in vacuum to obtain a residue (229 g) which was decoloured with activated charcoal in MeOH, filtered and evapd to yield 196 g brown syrup. The n—BuOH soln were also evapd in vacuum to yield 25 g yellow gums. The EtOAc fraction (166 g) was mixed with silica gel (180 g, 60～200 mesh) and subjected to CC over silica gel (1243 g, 200～300 mesh) eluting with CHCl3 and increasing proportions of MeOH—CHCl3 to obtain 1 (80 mg, 0.00103%), 4 (791 mg, 0.0102%), 3 (790 mg, 0.0102%), 2 (50 mg, 0.00064%). Some components were further purified by recrystallization and prep. TLC (silica gel).

ent—16β,17—Dihydroxykauran—19—oic acid (1) $C_{20}H_{32}O_4$, M 336; colourless plates (MeOH—$CHCl_3$), mp. 266～268℃; $[\alpha]_D^{25}$—88° (c 0.651, C_5H_5N); no UV absorption; IR $\nu_{max}^{KBr}cm^{-1}$: 3420, 3250, 1690, 1225, 1027; EIMS (20eV) m/z (%): 318[M—H_2O]$^+$(23), 305[M—CH_2OH]$^+$(100), 287[M—H_2O—CH_2OH]$^+$(25), 259[M—CH_2OH—HCOOH]$^+$(50), 121(68), 109(72), 95(56), 81(56), 43(57); ^{1}H NMR (C_5D_5N)δ: 4.13 and 4.04 (each 1H, ABd, J=10.8 Hz, 17—H2), 1.35 (3H, s, 18—Me), 1.19 (3H, s, 20—Me). The mp, mmp, [α]D, IR, and R_f value (TLC) of 1 are in agreement with those of authentic sample[6]. ^{13}C NMR data see Table 1.

siegesbeckioside (2) $C_{26}H_{44}O_8$, M 484; colourless needles (MeOH), mp. 276.5—277.5℃; $[\alpha]_D^{25}$—29.21° (c 0.290, C_5H_5N); no UV absorption; IR $\nu_{max}^{KBr}cm^{-1}$:3575, 3510, 3380, 2930, 2920, 1465, 1440, 1380, 1190, 1163, 1080, 1049, 1020, 921, 875; EIMS (20eV) m/z (%): 484[M+, no appearance], 466[M—H_2O]$^+$, 453[M—CH2OH]$^+$, 448[M—2H2O]$^+$, 435[M—H_2O—CH_2OH]$^+$, 430[M—3H_2O]$^+$, 417[M—CH_2OH—2H_2O]$^+$, 412[M—4H_2O]$^+$, 405, 399[M—CH_2OH—3H_2O]$^+$, 394[M—5H2O]$^+$, 377[M—5H2O—OH]$^+$, 333(2), 315(3),

304[M−Glucose]+(5), 291(33), 287[304−OH]+(22), 273[304−CH_2OH]+(46), 269[304−H_2O−OH]+(13), 255[304−CH_2OH−H_2O]+(11), 229(2), 43(100); ^1H NMR (C_5D_5N)δ: 4.80 (1H, d, J=7.76 Hz, Glc−1−H), 4.61 (1H, dd, J=11.64, 1.88 Hz, Glc−6−H), 4.46 (1H, dd, J=11.64, 5.20 Hz, Glc−6−H), 4.30−4.23(2H, m, Glc−H2), 4.09−4.00 (2H, m, Glc−H2), 4.13, 4.04 (each 1H, ABd, J=10.8 Hz, 17−H2), 3.75, 3.42 (each 1H, ABd, J=9.52 Hz, 18−H2), 1.00 (3H, s, 19−Me), 0.79 (3H, s, 20−Me). The Above−mentioned data of 2 are in agreement with those of authentic sample[6]. ^{13}C NMR data see Table 1.

pentaacetate of siegesbeckioside (2a) $C_{36}H_{54}O_{13}$, M 694; clubbed crystals (MeOH), mp. 171～172℃; $[\alpha]_D^{23}$ −61.14° (c 0.240, $CHCl_3$); no UV absorption; IRν_{max}^{KBr} cm^{-1}: 3555, 3500, 1745, 1443, 1380, 1370, 1250, 1225, 1040, 905, 620; EIMS (20eV) m/z (%): 694[M^+, no appearance], 677[M−OH]+(7), 635[M−OAc]+(2), 634[M−HOAc]+(3), 621[M−CH_2OAc]+(28), 617[M−OAc−H_2O]+(10), 616[M−H_2O−HOAc]+(25), 579[621−Ketene]+(4), 578[M−CH_2OAc−CH_3CO]+(12), 556[M−H_2O−2HOAc]+(5), 514[556−Ketene]+(6), 472[514−Ketene]+(4), 412[472−HOAc]+(2), 399[472−CH_2OAc]+(6), 346[M−Glc(Ac)$_4$]+, 331[346−CH_3]+, 315[346−CH_2OH]+, 286[346−HOAc]+, 255[286−CH_2OH]+(12), 229(5), 169(30), 43(100); ^1H NMR (C_5D_5N)δ: 5.71 (1H, t, J=9.56 Hz, Glc−H), 5.49, 5.44 (each 1H, ABd, J=9.88 Hz, Glc−6−H_2), 4.84 (1H, d, J=7.92 Hz, Glc−1−H), 4.88, 4.61 (each 1H, ABd, J=11.16 Hz, 17−H_2), 4.64～4.40 (2H, m, Glc−H_2), 4.12 (1H, dd, J=8.22, 2.92 Hz, Glc−H), 3.57, 3.31 (each 1H, ABd, J=9.22 Hz, 18−$_H$2), 2.14 (3H, s, OAc), 2.06 (6H, s, 2×OAc), 2.02 (3H, s, OAc), 2.01 (3H, s, OAc), 0.99 (3H, s, 19−Me), 0.77 (3H, s, 20−Me). The mp, mmp, [α]D, IR, and R_f value (TLC) of **2a** are in agreement with those of authentic sampl(Xiong *et al*, 1989). $_{13}C$ NMR data see Table 1.

darutoside (3) $C_{26}H_{44}O_8$, M 484; white amorphous powder (MeOH−$CHCl_3$), mp. 234～237℃; no UV absorption; IRν_{max}^{KBr} cm^{-1}: 3400−3360, 2940, 2870, 2850, 1630, 1450, 1375, 1160, 1072, 1025, 1010, 880; EIMS (70eV) m/z (%): 484[M^+, no appearance], 440, 423[M−CH(OH)CH_2OH]+(2), 346(100), 331, 316(13), 301(18), 271(16), 243[M−Glucose−CH(OH)CH_2OH]+(9), 229(22), 217, 205(14), 189, 128, 115, 105, 91, 77, 43(39); ^1H NMR (C_5D_5N)δ: 5.39 (1H, br s, 14−H), 4.84 (1H, d, J=7.68 Hz, Glc−1−H), 4.51 (1H, dd, J=9.84, 1.88 Hz, Glc−H), 4.51～4.33 (5H, m, 15−H, 16−H_2, Glc−H_2), 4.33 (1H, dd, J=11.32, 5.24 Hz, Glc−H), 4.21～3.91(2H, m, Glc−H_2), 3.52 (1H, dd, J=11.58, 3.50 Hz, 3(−H), 1. 19 (3H, s, 17−Me), 1.14(3H, s, 18−Me), 0.88 (3H, s, 20−Me), 0.67 (3H, s, 19−Me). The Above−mentioned data of 3 are in agreement with those of authentic sample(Dong *et al*, 1989). ^{13}C NMR data see Table 1.

hexaacetate of darutoside (3a) $C_{38}H_{56}O_{14}$, M 736; colourless needles (MeOH), mp. 88.5～89.5℃; no UV absorption; IRν_{max}^{KBr} cm^{-1}: 1750, 1640, 1370, 1250, 1225, 1090, 1040, 910, 870, 755, 630, 605; ^1H NMR (C_5D_5N)δ: 5.72 (1H, t, J=9.54 Hz, Glc−H), 5.47～5.35 (3H, m, 16−H, Glc−6−H_2), 5.27 (1H, br s, 14−H), 4.93 (1H, d, J=7.96 Hz, Glc−1−H), 4.63～4.40 (3H, m, 16−H′, Glc−H_2), 4.30 (1H, dd, J=11.62, 9.14 Hz, 15−H), 4.09 (1H, dd, J=9.94, 4.76 Hz, Glc−H), 3.40 (1H, dd, J=11.70, 3.86 Hz, 3(−H), 2.13 (6H, s, 2×OAc), 2.04 (3H, s, OAc), 2.03 (3H, s, OAc), 2.00 (3H, s, OAc), 1.98 (3H, s, OAc), 1. 13 (3H, s, 17−Me), 1.03(3H, s, 18−Me), 0.85 (3H, s, 20−Me), 0.84 (3H, s, 19−Me). 13C NMR data see Table 1.

daucosterol (4) $C_{35}H_{60}O_6$, white amorphous powder (MeOH−$CHCl_3$), mp. 276℃ (dec.); no UV absorption; IRν_{max}^{KBr} cm^{-1}: 3450−3360, 2930, 2867, 1457, 1435, 1374, 1362, 1162, 1104, 1070, 1020; The mp, mmp, $[\alpha]_D$, IR, and R_f value (TLC) of 4 are in agreement with those of authentic sample(Xiong *et al*, 1992).

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